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Rationality of Drug Administration in Patients with Diabetes Mellitus at Royal Prima Hospital Medan

Graida Tsuraiya Lubis, Nerly Juli Pranita Simanjuntak*, Razoki

Universitas Prima Indonesia

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*Correspondence: Nerly Juli Pranita Simanjuntak
Email: nerlyjulisimanjuntak24@gmail.com

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Abstract: Acute and chronic diseases caused by poor lifestyle choices or genetics are becoming more common over time and do not seem to be decreasing each year. This study aims to determine whether the treatment of type 2 diabetes mellitus patients with or without hypertension at Royal Prima Medan Hospital is appropriate. Descriptive research methodology, namely cross-sectional data, was used in this study. Retrospective data collection was conducted using information from medical records at one of the Royal Prima Medan University Hospitals from November 2023 to April 2024. Based on 93 medical records, the findings showed that the right drug, right indication, and right dose were all 100% rational. Moderate drug interactions accounted for 67% of all drug interactions, major interactions 18%, and minor interactions 15%. In conclusion, Royal Prima University Hospital in Medan had 100% rational medical data for the period November 2023-April 2024.

Keywords: Drug Rationality, Diabetes Mellitus Type 2, Hospital

Introduction

The number of cases of acute and chronic diseases caused by poor lifestyle choices or genetic factors is increasing over time and does not seem to decrease each year. Diabetes mellitus (DM) is one example of a chronic disease. When the pancreas cannot produce enough insulin or the body does not use insulin efficiently, the condition causes chronic diabetes mellitus (WHO, 2022).

One of the current global health problems is diabetes mellitus, a chronic disease that arises when insulin production is not normal or not performing as it should. Type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes mellitus, as well as other types are divisions of the disease that can be grouped based on their etiology (PERKENI, 2021). Insulin levels in people with type 2 diabetes can be below normal, the norm, or exceed normal, which allows them to avoid the need for insulin (Setiawan, 2021). Type 2 diabetes Non Insulin Dependent Diabetes Mellitus (NIDDM) is the most common type of diabetes (Arsanti et al., 2020).

Various variables, including both modifiable and immutable risk factors, contribute to the increasing number of patients with type 2 diabetes. Blood glucose can be well controlled through proper parameter criteria examination procedures, such as blood glucose levels in the range of 80-100 mg/dL during fasting, if two hours after eating the figure reaches 80-144 mg/dL, blood pressure <130/80 mmHg total cholesterol <200 mg/dL, HbA1C <6.5%, body mass index (BMI) 18.5 to 22.9 kg/m2, as well as triglycerides <150 mg/dL (Anggraini & Puspasari, 2019).

The American Diabetes Association (2023) states that glucose monitoring, medication administration, and lifestyle modification are part of a multidisciplinary approach to managing type 2 diabetes. Due to various clinical circumstances and potential side effects, drug administration to hospitalized patients is often more complicated.

According to the International Diabetes Federation, 537 million people between the ages of 20 and 79 worldwide have diabetes mellitus in 2021; this number is expected to rise to 643 million by 2030, then 15 years later in 2045 to 783 million. The incidence of diabetes, at 8.7%, is third in Southeast Asia. With 19.5 million people living with diabetes mellitus, Indonesia ranked fifth globally in 2021 and is the only country in Southeast Asia in the top 10 list of countries with the most people with diabetes (IDF, 2021).

Findings released by the Basic Health Research (Riskesdas) conducted in 2018, the majority of people in Indonesia with diagnosed diabetes mellitus are over 15 years old (Khairani, 2019).

Hypertension is one of the many problems facing the medical community. Since hypertension indicates a significant increase in blood pressure above the normal range, the general population calls it “high blood pressure”. This disease is known not to spread from individual to individual, so it is classified as a non-communicable disease (Mahyuni et al., 2021). In addition, another nickname that is often pinned on this disease is “silent killer”, because it shows minimal outward symptoms (Andari et al., 2020). Patients do not realize they have hypertension until they check their blood pressure, and the condition is often found without any symptoms (Nugraha et al., 2021).

Drug use is considered rational if the prescribed drug is consumed by the right patient, according to the indication of the disease, with a dose that is appropriate for the patient's condition, through the right method, and the patient can afford it (Dutta, 2019). Treatment for diabetes mellitus through drugs must be rational because irrational use of drugs can have a detrimental impact on the wearer, which can affect the quality of treatment, waste, dependence, and harmful side effects (Handayati, 2019). According to research by Razoki

et al. (2023) in one of the hospitals in Medan City, 54% of 13 prescriptions experienced drug interactions.

Based on the factors mentioned above, diabetes mellitus requires very logical therapeutic treatment. In addition to knowing the pharmacological drugs that best suit the disease conditions of diabetic patients, we must also understand the underlying pathophysiology. Treatment for diabetes mellitus must be reasonable to produce optimal therapeutic results. Drug selection can be more optimal if the drug is given according to the indication and condition of the patient.

Methodology

To assess the rationality of drug administration in patients with type 2 diabetes mellitus who seek treatment at Royal Prima Medan Hospital, this study used a descriptive method with a retrospective approach. To determine whether the pharmaceutical therapy provided was in accordance with applicable treatment recommendations, this study was conducted by examining patient medical record documents from November 2023 to April 2024. By using a retrospective approach, researchers can evaluate based on actual data that has occurred without having an impact on the patient's therapeutic course. The information evaluated in this case includes dose, frequency, mode of administration, and the presence of drug interactions.

With formal approval from the hospital and advice from the Faculty of Medicine, Dentistry, and Health Sciences of Universitas Prima Indonesia, this study was conducted in the inpatient department of Universitas Prima Medan Hospital. All inpatients diagnosed with type 2 diabetes mellitus, both those who also suffered from hypertension, became the study population. Purposive sampling, which is based on certain factors and criteria, was used for the sampling process. Patients with a diagnosis of type 2 diabetes mellitus, patients with a diagnosis of type 2 diabetes mellitus and hypertension, hospitalized patients, patients on antidiabetic drug therapy alone or together with antihypertensive drugs, and patients with complete medical records were eligible to participate in the study. Patients using insulin or suffering from type 1 diabetes mellitus, patients who were accidentally discharged or died during treatment, and patients with insufficient medical record data were excluded.

For processing and analysis, the data obtained were then entered into Microsoft Excel 2016 worksheets. Data editing, selection of data based on the variables under study, and assessment of drug rationality using predefined criteria were part of the analysis stage. Appropriate indication, drug, dosage, and attention to drug interactions are some of these

requirements. Using reliable internet resources such as Drugs.com, drug interactions are analyzed and classified as significant, moderate, or minor depending on their severity. The 2021 therapeutic guidelines from PERKENI (Indonesian Endocrinology Society), which serves as the benchmark for the treatment of type 2 diabetes mellitus in Indonesia, were consulted to further examine the evaluation findings.

Each component of rationality was evaluated for each eligible patient sample. Medicines were considered to be used rationally when therapy was administered according to the clinical indication, the appropriate type of drug was selected based on treatment guidelines, the dose was within the appropriate therapeutic range, and potential interactions with other drugs were considered. In addition, the reasoning component includes consideration of patient-specific variables including age and other comorbidities, as well as accuracy in the method of administration.

Upholding research ethics, protecting the confidentiality of patient identity, and avoiding risks or adverse effects on patients are the guiding principles of the entire research process. It is hoped that this study will help improve the standard of clinical pharmacy services and serve as a basis for assessing hospital drug policies. In addition, the findings from this study may increase the knowledge of healthcare professionals regarding the value of judicious drug use in improving patient safety and efficacy.

Results and Discussion

A. Patient Characteristics

Tabel 1. Distribution of characteristics of type II DM patients with hypertension

Patient characteristics	Patient encounter	Persentase (%)
Gender		
Female	66	71%
Male	27	29%
Age		
10 – 20 Year	3	3%
30 – 40 Year	12	13%
50 – 60 Year	58	62%
70 – 80 Year	20	22%
Presence of comorbidities		
Without comorbidities	30	32%
With comorbidities	63	68%

Table 1 above shows that females make up 71% of patients with type 2 diabetes mellitus and hypertension, while males make up 29%. This finding indicates that there are more female patients than male patients. Female respondents are 2.15 times more likely to

suffer from type 2 diabetes mellitus compared to male respondents, according to Galita and Septianingrum (2022). This is due to the fact that women usually consume foods that contain many risk factors, such as sugar and low physical activity can also increase the risk. Women are more likely to gain weight in some parts of the body due to hormonal changes after menopause (premenstrual syndrome), which increases the risk of type 2 diabetes mellitus. This study also supports research showing that female patients are twice as likely to have poor nutrition management adherence (Hestiana & Dita, 2022).

It has been shown that the hormones progesterone and estrogen increase the body's insulin response (Zulkarnain, 2021). After menopause, the body's ability to react to insulin decreases as estrogen and progesterone levels decrease. Women's weight, which is usually below ideal, is another factor that can reduce the sensitivity of the insulin response. Because of this, women are more likely to develop diabetes than men.

Based on age, this study showed that 62% of patients with type 2 diabetes mellitus and hypertension were elderly, followed by seniors (22%), adults (13%), and adolescents (3%). Because of the higher prevalence of glucose intolerance due to degenerative factors that inhibit the body's ability to regulate glucose, respondents with an age exceeding 45 years are more likely to develop type 2 diabetes mellitus than individuals who are not yet 45 years old. According to other studies, individuals with type 2 diabetes mellitus are more susceptible to acute and chronic diseases due to their parents' unhealthy lifestyles (Scarton et al., 2023). According to Zulkarnain (2021) when individuals whose age is in the 55-64 year range and diagnosed with type 2 diabetes have a reduction in life expectancy of 8 years.

Another finding can be seen in the results of research (Laili et al., 2022), proving the majority of individuals with type 2 diabetes are between 56 to 65 years old, with 45 respondents (45%) in that age group and 33 people (33%) for those whose age exceeds 65 years. The majority of DM patients are in their 40s to 60s. In addition, the majority of patients with type 2 DM are elderly, in accordance with research findings (Anisawati et al., 2023).

Diabetes mellitus usually develops in people who are at a vulnerable age, especially those who are obese and over 45 years old. This makes insulin in the body insensitive, and degenerative factors of decreased body function can increase the risk of developing diabetes mellitus and developing tolerance to glucose levels, especially the capacity of beta cells to produce insulin from glucose metabolism. People will face a sharp decline in physiological function when they reach the age of over 45 years due to the increasing shrinkage of pancreatic beta cells (Dian et al., 2022).

Thirty patients (32%) with a history of type 2 diabetes mellitus without comorbidities formed the basis of this investigation. However, 63 patients (68%) had a history of type 2 diabetes mellitus along with comorbid conditions, such as hypertension for example. Sharma's research (2020) suggests that the presence of risk factors in patients may be the first step in the relationship between type 2 diabetes mellitus and hypertension. Genetics, central obesity, environmental circumstances, nutrition, and physical exercise are some examples of such factors. The body will experience more oxidative stress and insulin resistance, early signs of diabetes mellitus, if these factors are present and some of them are impaired. Both increase the Renin-Angiotensin-Aldosterone system (RAAS) by causing hyperglycemia, dyslipidemia, and hyperinsulinemia.

B. Rational Use of Type II Antidiabetic Drugs Accompanied by Hypertension

1. Appropriate medication

Tabel 2. Data on Rationality of Drug Use Based on Appropriate Medication

Drug class	Biguanida	DPP-4 Inhibitor		Sulfonylurea			α-glucosidase Inhibitor	Thiazolinedone (TZD)	SGLT-2 Inhibitor
Type of medicine	Metformin	Sitagliptin	Linagliptin	Gliclazide	Glimipiride	Gliquidone	Acarbose	Pioglitazone	Dapagliflozin
Patients receiving drug theraphy	122	5	1	3	11	3	18	1	1
Patients who did not receive drug therapy	-	-	-	-	-	-	-	-	-
Rasionality	P	ü	ü	ü	ü	ü	ü	ü	ü

The groups of antidiabetic drugs used in RSU Royal Prima Medan are biguanide, DPP-4 inhibitors, sulfonylureas, α-glucosidase inhibitors, thiazolanidinedione, and SGLT-2 inhibitors, in line with the findings from the previously mentioned research. Metformin, a member of the biguanide group, primarily increases peripheral tissue glucose uptake while decreasing hepatic glucose synthesis. DPP-4 inhibitors work by preventing the release of glucagon. The main action of the sulfonylurea group is to increase the amount of insulin secreted by beta cells in the pancreas. The main function of the α-glucosidase inhibitor group is to block the task work of the alpha glucosidase enzyme of the gastrointestinal tract, so that the absorption of glucose that occurs in the small intestine will be inhibited. The main action of the thiazolidinedione (TZD) group is to reduce insulin resistance through increasing the levels of glucose-transporting proteins, and then inducing peripheral tissues to increase glucose uptake. The main mechanism of action of the SGLT-2 inhibitor group is

to increase glucose excretion through urine and block glucose reabsorption in the proximal tubules (PERKENI, 2021).

2. Right indication

Tabel 3. Data on Rationality of Drug Use Based on Appropriate Indication

Type 2 DM drug class	Type of medicine	Amount of medicine dispensed	Persentase(%)	Rasionality	
				Right indication	Inappropriate indication
Biguanida	**Metformin**	122	74%	ü	-
DPP-4 Inhibitor	**Sitagliptin**	5	30%	ü	-
	Linagliptin	1	0%	ü	-
Sulfonylurea	**Gliclazide**	3	2%	ü	-
	Glimipiride	11	7%	ü	-
	Gliquidone	3	2%	ü	-
α-glucosidase Inhibitor	**Acarbose**	18	11%	ü	-
Thiazolinedone (TZD)	**Pioglitazone**	1	0%	ü	-
SGLT-2 Inhibitor	**Dapagliflozin**	1	1%	ü	-
Total		**165**		**100%**	

The correspondence between the patient's clinical compliance and the use of medication is known as appropriate indication. The appropriate indication for treating type 2 diabetes mellitus is in line with the information contained in the patient's medical file, which includes blood sugar test findings greater than 200 mg/dL. There are three methods to diagnose diabetes mellitus: first, if the patient shows classic symptoms, the diagnosis can be made by looking at plasma glucose levels greater than 200 mg/dL. Second, the typical symptoms are fasting plasma glucose >126 mg/dL. Third, because it requires special preparation, patients are rarely given an oral glucose tolerance test (TTGO) (Ramdini et al., 2020).

The accuracy of drug administration between the doctor's indication and diagnosis is known as the right indication. Diagnosis is referred to as drug selection. In addition, the drug will not work properly if the diagnosis is incorrect. Whether or not a patient receives antidiabetic drugs depends on the support, namely the patient's blood sugar level, which shows the rationality of the appropriate prescription (PERMENKES, 2019).

Data on the rational use of antidiabetic drugs based on the right indication of the results obtained according to the medical records of hospitalized patients obtained the accuracy of 93 patients with type 2 diabetes showed 100% correct indications, in accordance with the results of the study mentioned above.

3. Right dose

Tabel 4. Data on Rationality of Drug Use Based on Right Dose

Type of medicine	Prescription dosage (mg)	Standard dosage (mg)	Amount	Description	
				Exactly	Inappropriate
Metformin	1x500 2x500 3x500	500-3000	18 33 71	 ü	-
Sitagliptin	1x100	100	5	ü	-
Linagliptin	1x5	5	1	ü	-
Gliclazide	1x80	40-80	3	ü	-
Glimipiride	1x2 2x4 3x4	1-8	6 3 2	ü	-
Gliquidone	2x30 3x30	15-120	1 2	ü	-
Acarbose	1x50 2x100 3x100	25-100	1 2 13	ü	-
Pioglitazone	1x30	15-30	1	ü	-
Dapagliflozin	1x10	5-10	1	ü	-
Total			**165**		

Proper dosing is when the drug is administered to the patient in a manner that is tailored to the therapeutic range, frequency of administration, dose, and route. In addition, the dose is modified based on the patient's weight and age. Pharmacological concentrations in the patient's plasma that are below the desired therapeutic range and doses that are too low resulting in unwanted side effects are two factors that contribute to inefficient pharmacological therapy (Triyadi et al., 2020).

The findings of the above-mentioned study on treatment based on the correct dose showed that 100% of patients received the correct dose. This is in accordance with the PERKENI 2021 criteria. To obtain the desired therapeutic effect of the drug, the dose should be administered according to the standard dose and not above or below the range.

C. Drug Interactions

Based on how often patients with type 2 diabetes mellitus and hypertension experience drug-related problems in the drug interaction category. Drug interactions can be divided into two groups: patients who experienced drug interactions (37 patients, or 40%) and patients who did not experience drug interactions (56 patients, or 60%).

Based on the severity, there were three categories of drug potency: moderate (up to 67%), severe (up to 18%), and mild (up to 15%).

One of the major oral antidiabetic drugs is metformin. It reduces triglycerides and LDL (Low Density Lipoprotein) cholesterol, suppresses hunger, improves insulin sensitivity, and stops the liver from producing glucose. For a number of reasons, metformin is the best choice for treating type 2 diabetes mellitus. Its cost and tolerability, its ability to lower blood sugar without causing weight gain by reducing hunger and tissue fat storage, and its compatibility with other oral antidiabetic drugs are the reasons (Noviyanto et al., 2023). The Indonesian Society of Endocrinology guidelines state that metformin is the most commonly prescribed drug and is the first-line treatment for individuals with type 2 diabetes, either alone or in combination. As a result, the drug that most often has the potential to interact with other drugs is metformin (Fitriani & Padmasari, 2022).

Diltiazem and bisoprolol is one of the drug combinations that may result in drug interactions. Combining diltiazem with bisoprolol may increase the likelihood of adverse symptoms such as headache, chest pain, shortness of breath, and increased or decreased heart rate. In addition, the use of these drugs is associated with a higher risk of developing depression (Drug Interaction Checker, 2022).

Hypotension is the result of a synergistic interaction between candesartan and spironolactone. Spironolactone and candesartan work together to treat hypertension in an additive manner. It is recommended to use a lower starting dose of candesartan and/or lower the dose of spironolactone to prevent or reduce hypotension (Hidayati et al., 2024).

Drug interaction between metformin and spirolactone. Spironolactone may interfere with diabetes management and increase blood sugar levels. Due to its effects on the kidneys, spironolactone may also increase the risk of lactic acidosis, which can occur when taking metformin-containing drugs. Due to the severe pharmacodynamic mechanisms, it is important to modify the dosage or check blood glucose levels regularly when taking the two drugs together (Drug Interaction Checker, 2022).

According to drug.com, it is possible that the combination of metformin and captopril will increase the risk or severity of lactic acidosis. Meanwhile, captopril may worsen the effects of metformin, thereby increasing the risk of hypokalemia, according to Baxter. Monitoring blood glucose levels and identifying early signs of hypokalemia are medications that can be used for patients. In addition, it is possible to modify the doses of metformin and captopril.

Captopril drug interaction with amlodipine. in which angiotensin-converting enzyme inhibitors (captopril) and calcium channel blockers (amlodipine) can have extra hypotensive effects. Although these drugs can often be taken together without incident, it is advisable

to check systemic blood pressure closely when taking them together, especially in the first one to three weeks of treatment (Agustin & Fitrianingsih, 2020).

Conclusion

According to this study, logical treatment criteria based on the parameters of indication, drug, and appropriate dose have been followed when administering drugs to patients with type 2 diabetes mellitus treated at Royal Prima University Hospital Medan. According to the PERKENI 2021 guidelines, the use of antidiabetic drugs such as metformin, sulfonylurea, and DPP-4 inhibitors has met the requirements of reasonableness. Ninety-three patients were found to have type 2 diabetes mellitus and/or hypertension, according to the findings of the study conducted using medical data. By gender, there were 27 men (29%) and 66 women (71%). The most prevalent condition, by diagnosis and comorbidity, was type 2 diabetes mellitus accompanied by hypertension, affecting up to 63 patients (68%) and 30 patients (32%), respectively. According to the data, up to 89 patients (73%) were taking biguanide antidiabetic drugs, specifically metformin. A total of 93 people (100%) could be identified based on the findings of the assessment of the rationality of antidiabetic drug use, including the right drug, the right indication and the right dose. It is good that this level of therapeutic rationality has been achieved. The rationale requirement has also been met by the use of drugs in patients with concomitant hypertension. The assessment of the rationale of drugs for diabetes mellitus and hypertension showed conformity with the current standard of care in terms of dose and type selection.

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